Prevalence of Chronic Kidney Disease in Adults with Type 2 Diabetes Mellitus

Serena KM Low, ¹*MBBS, MSc (Public Health)*, Chee Fang <u>Sum</u>, ²*FRCPI, FRCPE, FACE*, Lee Ying <u>Yeoh</u>, ³*MD, MRCP*, Subramaniam <u>Tavintharan</u>, ⁴ *FAMS, FRCP, MCI*, Xiao Wei <u>Ng</u>, ⁴*PhD (Food Science)*, Simon BM Lee, ⁵*MBBS, M Med (Family Med), MCFP*, Wern Ee <u>Tang</u>, ⁶*MBBS, M Med (Family Med), FCFP*, Su Chi Lim, ²*MBBS, MRCP, PhD*

Abstract

Introduction: Diabetes mellitus (DM) is a major cause of chronic kidney disease (CKD). The epidemiology of CKD secondary to type 2 DM (T2DM) (i.e. diabetic nephropathy (DN)) has not been well studied in Singapore, a multi-ethnic Asian population. We aimed to determine the prevalence of CKD in adult patients with T2DM. Materials and Methods: We conducted a cross-sectional study on patients (n = 1861) aged 21 to 89 years with T2DM who had attended the DM centre of a single acute care public hospital or a primary care polyclinic between August 2011 and November 2013. Demographic and clinical data were obtained from patients using a standard questionnaire. Spot urine and fasting blood samples were sent to an accredited hospital laboratory for urinary albumin, serum creatinine, HbA1c and lipid measurement. CKD was defined and classified using the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines and classification. Results: The distribution by risk of adverse CKD outcomes was: low risk, 47%; moderate risk, 27.2%; high risk, 12.8%; and very high risk, 13%. The prevalence of CKD in patients with T2DM was 53%. Variables significantly associated with CKD include neuropathy, blood pressure ≥140/80 mmHg, triglycerides ≥1.7 mmol, body mass index, duration of diabetes, HbA1c \geq 8%, age, cardiovascular disease, and proliferative retinopathy. Conclusion: CKD was highly prevalent among patients with T2DM in Singapore. Several risk factors for CKD are well recognised and amenable to intervention. Routine rigorous screening for DN and enhanced programme for global risk factors reduction will be critical to stem the tide of DN.

Ann Acad Med Singapore 2015;44:164-71

Key words: Albuminuria, Renal impairment, Risk factors

Introduction

According to the National Health Survey, the percentage of Singapore residents with diabetes mellitus (DM) aged between 18 and 69 years has risen from 8.2% in 2004 to 11.3% in 2010.^{1,2} DM can lead to a myriad of long-term health complications such as coronary heart disease, kidney failure and stroke.³ Of note, DM is a major cause of kidney failure.⁴ There is a rising trend of end-stage renal disease (ESRD) due to DM. The proportion of diabetics among new ESRD patients increased from 48.2% in 1999 to 63.5% in 2011.⁵ The problem of kidney failure arising from DM will be of even more concern as DM prevalence increases.

There are guidelines⁶⁻⁸ to facilitate detection and

Address for Correspondence: Dr Serena Low, Research Laboratory, Basement 1, Khoo Teck Puat Hospital, 90 Yishun Central, Singapore 768828.

Email: low.serena.km@alexandrahealth.com.sg

appropriate management of patients with chronic kidney disease (CKD). The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 clinical practice guideline for the evaluation and management of CKD has recently updated the original 2002 version with enhanced classification of CKD. This includes adding the cause and categories of albuminuria besides glomerular filtration rate (GFR) in the assessment, and refining GFR category 3 into 3a and 3b. The risk categorisation of CKD is reflected in the yearly rate of decline in renal function, e.g. GFR drop of $\leq 1 \text{ mL/min}/1.73\text{m}^2/\text{year}$ in subjects with low risk of CKD progression and $\geq 4 \text{ mL/min}/1.73\text{m}^2/\text{year}$ in those with high risk of CKD progression.⁶ It will be useful to

¹Clinical Services, Khoo Teck Puat Hospital, Singapore

²Diabetes Centre, Khoo Teck Puat Hospital, Singapore

³Department of Medicine, Khoo Teck Puat Hospital, Singapore

⁴Clinical Research Unit, Khoo Teck Puat Hospital, Singapore

⁵Yishun Polyclinic, Singapore

⁶National Healthcare Group Polyclinics, Singapore

understand the prevalence of the CKD based on the revised categories. Furthermore, information on the burden of CKD in DM patients in Singapore is limited although there has been extensive research on this group internationally.9-15 There were a few studies that examined the status of renal function among patients with diabetes in Singapore.¹⁶⁻¹⁸ For example, the Diabcare-Singapore 1998 study revealed abnormal levels of urinary protein (>500 mg/24 hours) in 16%, microalbuminuria in 36% and raised serum creatinine in 3% of the patients tested in 22 diabetes clinics from general hospitals and primary healthcare centres.¹⁵ While these studies have shed light on the renal status in terms of albuminuria and elevated creatinine, little is known about CKD prevalence among patients with DM using the KDIGO revised guidelines. We therefore undertook a study to determine the prevalence of CKD as well as its associated factors in patients with Type 2 DM (T2DM). We hope to establish a baseline profile for the risk of CKD outcome with the findings in order to develop future prevention and management strategies tailored to patients with T2DM.

Materials and Methods

Study Design

This is a cross-sectional study involving 1861 adult patients aged between 21 and 89 years with T2DM who attended the DM centre or a primary care polyclinic in the northern region of Singapore between August 2011 and November 2013. The polyclinics in Singapore provide medical care for acute and chronic conditions, medical examination, screening and other services. The DM centre is a one-stop centre located in Khoo Teck Puat Hospital (KTPH) for people with DM in the northern region of Singapore. It manages patients with DM with more complications that require a higher level of holistic care. The study was approved by the National Healthcare Group Domain Specific Review Board in Singapore and all patients signed written informed consent.

The exclusion criteria were as follows: T1DM, pregnancy, active inflammation, cancer, on non-steroid anti-inflammatory drugs (NSAIDS) on the day of the assessment, on oral steroids equivalent to >5 mg/day of prednisolone, fasting glucose <4.5 mmol or >15 mmol, HbA1c >12%, inability to give informed consent and insertion of pacemaker or any device that may be affected by electric current.

Measurement

Data on demographics, vascular risk factors, diabetic complications and medications were extracted from a standard questionnaire answered by all patients. Blood pressure was measured by trained nurses using a standard electronic sphygmomanometer. The measurement was done on the arm of the subject with an appropriate cuff in the sitting position, and an average of 3 readings was taken. High blood pressure (BP) was deemed as systolic blood pressure \geq 140 mmHg and/or diastolic blood pressure \geq 80 mmHg, taking reference from the 2014 American Diabetes Association (ADA) recommendations.¹⁹ Ankle pressure was measured after a 5-minute rest in supine position with a standardised Doppler ultrasonic device. Ankle brachial index (ABI) was calculated as the ratio of the higher of the 2 systolic pressures at the ankle to the higher of the right and left brachial artery pressures. Peripheral artery disease (PAD) was defined as present if the lower ABI < 0.9.^{20,21} Neuropathy was assessed using a neurothesiometer for vibration and a 5.07 (10 g) monofilament on non-calloused plantar sites for light touch. For monofilament assessment in the foot, the test is considered abnormal if a patient fails to feel at least 3 out of 10 sites. For neurothesiometer readings, a mean of 3 values greater than 25 volts indicates that the patient is at risk, and the test is considered as abnormal. Neuropathy was defined as the presence of an abnormal finding in monofilament or neurothesiometer testing. Retinopathy was ascertained from patients' medical record. If this was absent, the patient was asked for the information through questionnaire.

Spot urine creatinine was obtained along with spot urine albumin and serum creatinine. An average reading for a maximum of 3 tests was obtained. Blood samples for HbA1c and lipids were also taken from the patients. The spot urine and blood samples were sent to the hospital laboratory accredited by the College of the American Pathologists (CAP) for measurement. The following assays or methods were used for measurement: Roche cobas® c501 immunoturibidmimetric assay for urinary albumin; Roche cobas[®] c501 enzymatic colorimetric test for serum creatinine, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-cholesterol), high-density lipoprotein cholesterol (HDL-cholesterol) and triglycerides (TG); and monoclonal antibody agglutination reaction using Siemens DCA Vantage® analyser for glycated haemoglobin (HbA1c). Lipid abnormalities were considered as follows: LDL-cholesterol ≥ 2.6 mmol/L (high LDL-cholesterol); HDL-cholesterol $\leq 1 \text{ mmol/L}$ in men or $\leq 1.3 \text{ mmol/L}$ in women (low HDL-cholesterol); TC ≥5.2 mmol/L (high TC); and TG \geq 1.7 mmol/L (high TG), taking references from the 2014 ADA recommendations.¹⁹

The Modification of Diet in Renal Disease (MDRD) formula was used to calculate the estimated GFR (eGFR).²² We are aware of another equation—the Chronic Kidney Disease Epidemiology (CKD-EPI) collaboration equations—formulated for the general population (i.e. not limited to T2DM). We have decided to adopt the MDRD

formula given the wealth of publications based on this equation. The KDIGO 2012 CKD guidelines defined albuminuria categories as normal or mildly increased, moderately increased and severely increased for urinary albumin to creatinine ratio (ACR) values of <30 mg/g, 30 to 300 mg/g and >300 mg/g respectively. In the KDIGO 2012 CKD Guidelines, CKD was defined by the presence of decreased GFR $<60 \text{ mL/min per } 1.73 \text{ m}^2$ or kidney damage as indicated by ACR $\geq30 \text{ mg/g}$ or other markers for more than 3 months.⁶ As we were unable to ascertain if the above abnormalities persisted for more than 3 months, we defined CKD as GFR $<60 \text{ mL/min per } 1.73 \text{ m}^2$ or ACR $\geq30 \text{ mg/g}$ in our study.

Statistical Analysis

Categorical data were expressed as number (percentage) and continuous data as means \pm standard deviation (SD) unless otherwise stated. Differences in patient characteristics, risk factors, medications and complications among categories of risk for CKD outcomes (low, moderate and high/very high risk) were studied using chi-square test for categorical variables, and one-way ANOVA or Kruskal Wallis for continuous variables where appropriate. Logistic regression was used to estimate the odds ratio (OR) for the association between patient characteristics and CKD. Variables were subsequently included in the age-adjusted multivariable logistic regression if P < 0.1 in the bivariate logistic regression. Statistical significance is taken at P<0.05. Statistical analysis was performed using STATA version 13 (STATA Corporation, College Station, Texas).

Results

Table 1 shows the baseline characteristics of the 1861 patients with T2DM as follows: mean age, 57.5 ± 10.7 years; 50.1% males; duration of diabetes, 10 years (4 years to 16 years), mean body mass index (BMI), 27.7 ± 5.2 kg/m²; mean HbA1c, 7.5% (6.8% to 8.5%); 46.6% with BP \geq 140/80 mmHg; 17.1% with high TC; 51.5% with high LDL-cholesterol; 37.9% with low HDL-cholesterol; and 35.9% with high TG.

The distribution by risk for outcome of CKD was as follows: low risk, 47%; moderate risk, 27.2%; high risk, 12.8%; and very high risk, 13%. Of the 1861 patients, 53% had CKD, 21.4% had GFR <60 mL/min per 1.73 m² and 48% had ACR \geq 30 mg/g. Figure 1 shows the distribution by GFR and albuminuria categories.

The characteristics of patients by CKD risk categories are shown in Table 1. Patients with moderate or high/very high risk of CKD tended to be older, of Malay ethnicity, had longer duration of diabetes, with higher BMI, HbA1c \geq 8%, BP \geq 140/80 mmHg, low HDL cholesterol, and high TG (*P* <0.001 for all).

Compared to the low risk for CKD group, the moderate and high/very high risk groups had higher proportions of use of insulin, aspirin, angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB) and statins (P < 0.001 for all). In terms of complications, patients in the moderate and high/very high risk groups were more likely to have proliferative retinopathy, neuropathy and CVD (which includes heart attack, blockade of arteries, balloon angioplasty of blocked artery of the heart, bypass operation, stroke or PAD (P < 0.001 for all).

Risk Factors for CKD

The significant risk factors in the multivariable model were neuropathy (OR 3.64, 95% CI, 1.99 to 6.65); BP \geq 140/80 mmHg (OR 2.45, 95% CI, 1.86 to 3.23), TG \geq 1.7 mmol/L (OR 1.77, 95% CI, 1.3 to 2.4), BMI (OR 1.07, 95% CI, 1.04 to 1.1); duration of DM (OR 1.05, 95% CI, 1.03 to 1.07), HbA1c \geq 9% (OR 1.8, 95% CI, 1.16 to 2.78), age (OR 1.02, 95% CI, 1 to 1.03), HBA1c 8% to <9% (OR 1.57, 95% CI, 1.06 to 2.34); CVD (OR 1.45, 95% CI, 1.02 to 2.05) and proliferative retinopathy (OR 1.79, 95% CI, 1 to 3.2) (Table 2).

Discussion

The prevalence of CKD among T2DM, defined as ACR \geq 30 mg/g or GFR <60 mL/min per 1.73 m², was reported to range from 27.9% to 77% in other countries.9-15 The wide variation in the burden of CKD in these studies could be due to differences in CKD definition or patient profiles such as ethnicity and healthcare setting, i.e. primary care catchment versus hospital care. In our study, 53% of T2DM patients had CKD as defined by KDIGO. The higher prevalence of CKD in our study population as compared to most of the earlier studies could be attributed to the more advanced cases managed in KTPH DM Centre (i.e. referral bias to a secondary hospital). It may also reflect the high (and rising) burden of diabetes in an urbanised society like Singapore—our latest national health survey suggested that approximately 11.3% of the adult population had diabetes.² Although it is likely that most of the CKD is secondary to DM, we do not know the proportion of individuals whose CKD can be attributable to other causes such as hypertension, IgA nephropathy and chronic glomerulonephritis. Other possible reasons for the relatively high prevalence of CKD in our study populations include: Asian's ethnic related susceptibility to diabetic nephropathy;²³ seniority of study population and age-dependent eGFR formula;²⁴ high burden of atherosclerosis and arterial calcification.²⁵ Nonetheless, the high prevalence of CKD in our study constitutes a significant public health concern as it not only

Table 1. Characteristics of Patients by CKD Risk Categories (Low, Moderate and High/Very High)							
Characteristics	All* (n = 1861)	Low Risk* (n = 875)	Moderate Risk* (n = 506)	High/Very High Risk* (n = 480)	P Value		
Age (years)	57.5 ± 10.7	55.8 ± 10.8	57.6 ± 10.4	60.5 ± 10.3	< 0.001		
Gender							
Male	932 (50.1)	428 (48.9)	240 (47.4)	264 (55)	0.038		
Ethnic group					< 0.001		
Chinese	950 (51.1)	464 (53)	236 (46.6)	250 (52.1)			
Malay	427 (22.9)	152 (17.4)	135 (26.7)	140 (29.2)			
Indian	428 (23)	228 (26.1)	120 (23.7)	80 (16.7)			
Others	56 (3)	31 (3.5)	15 (3)	10 (2.1)			
Duration of diabetes (years)	10 (4 - 16)	7 (3 – 12)	10 (4 - 16.5)	15 (9 – 20)	0.0001		
Control of Risk Factors							
Smoking history					0.012		
Never	1570 (84.6)	755 (86.3)	422 (83.7)	393 (82.4)			
Ex-smoker	131 (7.1)	54 (6.2)	29 (5.8)	48 (10.1)			
Current smoker	155 (8.4)	66 (7.5)	53 (10.5)	36 (7.6)			
Body mass index (kg/m ²)	27.7 ± 5.2	27.1 ± 4.9	28.4 ± 5.5	28.2 ± 5.2	< 0.001		
Waist circumference (cm)	95.3 (88.1 - 104.5)	93.6 (87.1 - 103.1)	96.8 (89.1 - 106.7)	96.5 (88.4 - 104.2)	0.0006		
HbA1c (%)	7.5 (6.8 - 8.5)	7.2 (6.7 – 8.2)	7.6 (6.9 – 8.7)	8 (7.1 – 9)	0.0001		
HbA1c group					< 0.001		
<7%	575 (30.9)	334 (38.2)	140 (27.7)	101 (21)			
7% to <8%	588 (31.6)	292 (33.4)	157 (31)	139 (29)			
8% to <9%	365 (19.6)	135 (15.4)	111 (21.9)	119 (24.8)			
≥9%	333 (17.9)	114 (13)	98 (19.4)	121 (25.2)			
Systolic BP (mmHg)	139 (127 – 152)	133 (123 – 146)	141 (130 – 153)	149 (136 – 164)	0.0001		
Diastolic BP (mmHg)	79.1 ± 9.6	77.9 ± 8.8	80.6 ± 9.6	79.7 ± 10.7	< 0.001		
$BP \ge 140/80 mmHg$	568 (46.6)	198 (33.8)	179 (53.9)	191 (63.5)	< 0.001		
Total cholesterol (mmol/L)	4.3 (3.8 – 4.9)	4.3 (3.8 – 4.9)	4.3 (3.8 – 4.9)	4.4 (3.8 – 5)	0.189		
Total cholesterol ≥5.2 mmol/L	318 (17.1)	131 (15)	91 (18)	96 (20)	0.05		
HDL cholesterol in men (mmol/L)	1.2 (1 – 1.3)	1.2 (1 – 1.4)	1.2 (1 – 1.3)	1.1 (0.9 – 1.3)	0.0125		
HDL cholesterol in women (mmol/L)	1.4 (1.2 – 1.6)	1.4 (1.2 – 1.6)	1.3 (1.1 – 1.6)	1.3 (1.1 – 1.5)	0.0001		
HDL cholesterol $\leq 1 \text{ mmol/L}$ in men or $\leq 1.3 \text{ mmol/L}$ in women	704 (37.9)	288 (32.9)	209 (41.3)	207 (43.2)	<0.001		
LDL cholesterol (mmol/L)	2.6 (2.2 - 3.2)	2.6 (2.2 - 3.2)	2.6 (2.2 - 3.2)	2.7 (2.2 - 3.3)	0.547		
LDL cholesterol ≥2.6 mmol/L	957 (51.5)	444 (50.7)	256 (50.6)	257 (53.7)	0.534		
Triglycerides (mmol/L)	1.4 (1 – 2)	1.3 (1 – 1.8)	1.4 (1.1 – 1.9)	1.7 (1.2 – 2.3)	0.0001		

BP: Blood pressure; CKD: Chronic kidney disease; CVD: Cardiovascular disease; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; PAD: Peripheral artery disease

187 (37)

242 (50.5)

< 0.001

239 (27.3)

668 (35.9)

*Categorical variables were expressed as numbers (%). Continuous variables were expressed as mean ± SD for normally distributed variables or median (25% and 75% quartile) for non-normally distributed variables.

Triglycerides $\geq 1.7 \text{ mmol/L}$

Characteristics	All* (n = 1861)	Low Risk* (n = 875)	Moderate Risk* (n = 506)	High/Very High Risk* (n = 480)	P Value
Medications					
Use of insulin	536 (29)	155 (17.8)	138 (27.4)	243 (51.1)	< 0.001
Use of aspirin	427 (23.1)	130 (14.9)	114 (22.8)	183 (38.4)	< 0.001
Use of ace-inhibitor or angiotensin receptor blocker	1105 (59.5)	355 (40.6)	359 (71.1)	391 (81.8)	< 0.001
Use of statins	1507 (81.2)	672 (77)	415 (82.3)	420 (87.9)	< 0.001
Complications					
Retinopathy					< 0.001
Normal	1284 (71.7)	669 (79.6)	366 (75.8)	249 (53.1)	
Non-proliferative	327 (18.3)	138 (16.4)	77 (15.9)	112 (23.9)	
Proliferative	181 (10.1)	33 (3.9)	40 (8.3)	108 (23)	
PAD	250 (14.4)	80 (9.7)	69 (14.6)	101 (23.2)	< 0.001
Neuropathy	171 (9.6)	30 (3.6)	35 (7.2)	106 (23.7)	< 0.001
PAD and neuropathy	46 (2.6)	5 (0.6)	8 (1.6)	33 (7.3)	< 0.001
Heart attack	32 (3.6)	5 (1.2)	9 (3.6)	18 (8.2)	< 0.001
Blockade of arteries to the heart	84 (9.7)	25 (6.3)	27 (11)	32 (14.6)	0.003
Balloon angioplasty of blocked artery of the heart	49 (5.6)	16 (3.9)	15 (6)	18 (8.1)	0.084
Bypass operation	42 (4.8)	12 (2.9)	17 (6.8)	13 (5.9)	0.051
Stroke	29 (3.3)	8 (2)	9 (3.6)	12 (5.4)	0.062
CVD	356 (20)	117 (13.9)	106 (22.1)	133 (29.2)	< 0.001

Table 1. Characteristics of Patients by CKD Risk Categories (Low, Moderate and High/Very High) (Con't)

BP: Blood pressure; CKD: Chronic kidney disease; CVD: Cardiovascular disease; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; PAD: Peripheral artery disease

*Categorical variables were expressed as numbers (%). Continuous variables were expressed as mean \pm SD for normally distributed variables or median (25% and 75% quartile) for non-normally distributed variables.

				Persistent Albuminuria Categories			
				A1	A2	A3	
				Normal to Mildly Increased	Moderately Increased	Severely Increased	
	-	-	-	<30 mg/g n (%)	30 – 300 mg/g n (%)	>300 mg/g n (%)	Total
	G1	Normal or high	≥90	469 (25)	256 (14)	55 (3)	780 (42)
3 m²)	G2	Mildly decreased	60 - 89	406 (22)	188 (10)	88 (5)	682 (37)
in per 1.7	G3a	Mildly to moderately decreased	45 – 59	62 (3)	68 (4)	49 (3)	179 (10)
ies (ml/m	G3b	Moderately to severely decreased	30 - 44	28 (2)	53 (3)	37 (2)	118 (6)
ategor	G4	Severely decreased	15 – 29	3 (0)	19 (1)	48 (3)	70 (4)
GFR C	G5	Kidney failure	<15	0 (0)	1 (0)	31 (2)	32 (2)
			Total	968 (52)	585 (31)	308 (17)	1861 (100)

Low risk
Moderate ris

High risk Very high risk Fig. 1. Distribution by GFR and albuminuria categories (n = 1861). Classification is based on KDIGO 2012 Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease.⁶ GFR: Glomerular filtration rate

Table 2. Factors Associated with CKD Status

Chamadaniatian	OR (95% CI) P Value			
	Bivariate	Multivariable*		
Age (per year)	1.03 (1.02 – 1.04) <0.001	1.02 (1 – 1.03) 0.016		
Male vs female	1.09 (0.91 – 1.31) 0.343			
Duration of diabetes (per year)	1.06 (1.05 – 1.07) <0.001	1.05 (1.03 – 1.07) <0.001		
Chinese vs others	1.3 (0.76 – 2.23) 0.344	1.14 (0.48 – 2.73) 0.769		
Malays vs others	2.24 (1.28 - 3.94) 0.005	1.5 (0.61 – 3.7) 0.374		
Indians vs others	1.09 (0.62 - 1.9) 0.769	0.78 (0.32 - 1.92) 0.591		
Ex-smoker vs non-smoker	1.32 (0.92 – 1.9) 0.131			
Current smoker vs non-smoker	1.25 (0.9 – 1.74) 0.191			
Body mass index (per kg/m ²)	1.05 (1.03 – 1.07) <0.001	1.07 (1.04 – 1.1) <0.001		
HbA1c 7% to <8% vs HbA1c <7%	1.4 (1.11 – 1.77) 0.004	1.04 (0.73 – 1.47) 0.835		
HbA1c 8% to <9% vs HbA1c <7%	2.36 (1.8 - 3.09) < 0.001	1.57 (1.06 – 2.34) 0.025		
HbA1c ≥9% vs HbA1c <7%	2.66 (2.01 - 3.52) < 0.001	1.8 (1.16 – 2.78) 0.008		
BP≥140/80 mmHg	2.76 (2.18 - 3.48) < 0.001	2.45 (1.86 - 3.23) <0.001		
Total cholesterol \geq 5.2 mmol/L	1.33 (1.04 – 1.7) 0.021	1.02 (0.7 – 1.5) 0.908		
HDL cholesterol $\leq 1 \text{ mmol/L in men or } \leq 1.3 \text{ mmol/L in women}$	1.49 (1.23 – 1.8) <0.001	1.25 (0.92 - 1.68) 0.153		
LDL cholesterol \geq 2.6 mmol/L	1.05 (0.88 – 1.27) 0.564			
Triglycerides $\geq 1.7 \text{ mmol/L}$	2.05 (1.69 - 2.5) <0.001	1.77 (1.3 – 2.4) <0.001		
Non-proliferative retinopathy vs normal	1.5 (1.17 – 1.9) 0.001	0.93 (0.64 - 1.35) 0.703		
Proliferative retinopathy vs normal	4.88 (3.29 - 7.23) <0.001	1.79 (1 – 3.2) 0.049		
Neuropathy	4.81 (3.21 - 7.22) <0.001	3.64 (1.99 - 6.65) < 0.001		
CVD	2.13 (1.67 - 2.72) <0.001	1.45 (1.02 – 2.05) 0.039		

CKD: Chronic kidney disease; CVD: Cardiovascular disease; HDL: High-density lipoprotein; LDL: Low-density lipoprotein

*The multivariable model includes age, ethnic group, duration of diabetes, BMI, HbA1c group, BP \ge 140/80 mmHg, total cholesterol \ge 5.2 mmol/L, HDL

 $cholesterol \leq 1 mmol/L in men or \leq 1.3 mmol/L in women, triglycerides \geq 1.7 mmol/L, history of retinopathy, history of neuropathy, and history of CVD.$

heralds the rise of ESRD, but also an in-tandem rise in other closely associated comorbidities such as cardiovascular diseases. This may contribute to the rising cost of health care for serious chronic conditions in Singapore. It also highlights the importance of routine rigorous screening for CKD and subsequently aggressive intervention to retard renal progression. In corollary, relevant health education targeting T2DM patients, their families and care providers will be vital.²⁴

Our study has demonstrated that serious comorbidities such as neuropathy, cardiovascular disease and proliferative retinopathy are highly prevalent among individuals with CKD (Table 2). Of note, a study in Japan showed that diabetic micro and macroangiopathies were more prevalent in the later stages of both GFR and albuminuria.¹⁵ Therefore, simultaneous screening for these comorbidities should be carefully considered and acted upon when clinically indicated. Our data reiterated that major traditional risk factors (e.g. smoking, hyperglycaemia, dyslipidaemia and hypertension) are associated with CKD. These risk factors are likely to be causal because several landmark clinical trials have provided strong evidence to suggest that diligent control of these risk factors can retard renal progression as well as ameliorate the risk for cardiovascular disease.²⁶⁻²⁸ Therefore, our data reminded us of the need to strengthen our diabetes care programme to meet the rising challenge of CKD.

Our study shows that only 30.9% of patients had met the target of HbA1c <7% and 53.4% had BP <140/80 mmHg. The lipid targets were achieved in more than 60% of patients, with the exception of LDL-cholesterol where 48.5% met the target of <2.6 mmol/L. Our results on treatment targets are comparable with findings from other countries. The National Healthcare Quality Report from the US shows that the proportions of adults aged 40 and above with diagnosed DM who achieved HbA1c <7% and BP <140/80 mmHg were 52% and 65% respectively,²⁹ whereas the 2011 to 2012 National Diabetes Audit report from the UK showed that proportions of patients in England and Wales who achieved HbA1c <6.5% and <7.5%, BP <140/80 mmHg and cholesterol <5 mmol/L were 24.7%, 62.7%, 48.1% and 77% respectively.³⁰ Therefore, it is important to continue to strive towards optimising risk factor management among our T2DM population. Having said so, we are cognisant of the possibility that not meeting the traditionally recommended glycaemic target of HbA1c <7% may reflect the evolving paradigm shift in clinical practice guidelines, which recommend less intensive glycaemic control in population with heavy comorbidities such as CKD or CVD because of the paradoxical increase in mortality that is probably related to treatment-associated severe hypoglycaemia.¹⁹

There are limitations in our study. Firstly, the crosssectional design of our study precludes any causal inference between CKD and their risk factors. Secondly, it is possible for misclassification on retinopathy to occur when the information was obtained from questionnaire. Another limitation was that our study was confined to only patients with T2DM in the polyclinics and diabetes centre in a local hospital, and hence the findings cannot be generalised to the general diabetes patient population, including those with T1DM.

To the best of our knowledge, this is the first study on the prevalence of CKD and its risk outcomes in patients with T2DM using the recent KDOQI 2012 criteria in Singapore. The findings have established the baseline profile of CKD prevalence and CKD risks amongst patients with T2DM for future management and prevention strategies. They will help clinicians appreciate the magnitude of CKD among patients with T2DM and exercise vigilance in diabetes care, especially in those known risk factors. It is hoped that our study will provide impetus for further research on renal complications in DM patients so as to improve clinical outcomes.

Conclusion

CKD is highly prevalent among patients with T2DM in Singapore. Several risk factors for CKD are well elucidated and amenable to interventions. Our data suggest substantial unmet challenges of CKD risk factors among T2DM population. Therefore, routine screening for renal impairment and enhanced programme for global risk factors reduction is important to stem the tide of CKD in T2DM.

Acknowledgement

The authors would like to thank Dr Tan Hwee Huan for her comments on the manuscript. The study was funded by National Medical Research Council, Program Project Grant (NMRC/PPG/AH(KTPH)/2011).

REFERENCES

- Ministry of Health, Singapore. National Health Survey 2004. Singapore, Ministry of Health, 2005.
- Ministry of Health, Singapore. National Health Survey 2010. Singapore, Ministry of Health, 2011.
- 3. Health Promotion Board, Singapore. Information paper on diabetes in Singapore. Singapore, Health Promotion Board, 2011.
- Vathsala A. Twenty-five facts about kidney disease in Singapore: in remembrance of World Kidney Day. Ann Acad Med Singapore 2007;36:157-60.
- Health Promotion Board, Singapore. Trends of end stage renal disease in Singapore. Singapore, Health Promotion Board, 2013.
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2013;3:1-150.
- The RenalAssociation. Detection, monitoring and care of patients with CKD [Internet]. Hampshire: the Renal Association; 2011. Available at: http:// www.renal.org/guidelines/clinical-practice-guidelines-committee#sthash. GN5rsYnj.dpbs. Accessed 20 February 2014.
- Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M, et al. Guidelines for the management of chronic kidney disease. CMAJ 2008;179:1154-62.
- Rodriguez-Poncelas A, Garre-Olmo J, Franch-Nadal J, Diez-Espino J, Mundet-Tuduri X, Barrot-De la Puente J, et al. Prevalence of chronic kidney disease in patients with type 2 diabetes in Spain: PERCEDIME2 study. BMC Nephrol 2013;14:46.
- Jia W, Gao X, Pang C, Hou X, Bao Y, Liu W, et al. Prevalence and risk factors of albuminuria and chronic kidney disease in Chinese population with type 2 diabetes and impaired glucose regulation: Shanghai diabetic complications study (SHDCS). Nephrol Dial Transplant 2009;24:3724-31.
- Lou QL, Ouyang XJ, Gu LB, Mo YZ, Ma R, Nan J, et al. Chronic kidney disease and associated cardiovascular risk factors in Chinese with type 2 diabetes. Diabetes Metab J 2012;36:433-42.
- Coll-de-Tuero G, Mata-Cases M, Rodriguez-Poncelas A, Pepió JM, Roura P, Benito B, et al. Chronic kidney disease in the type 2 diabetic patients: prevalence and associated variables in a random sample of 2642 patients of a Mediterranean area. BMC Nehrol 2012;13:87.
- de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. JAMA 2011;305:2532-9.
- Thomas MC, Weekes AJ, Broadley OJ, Cooper ME, Mathew TH. The burden of chronic kidney disease in Australian patients with type 2 diabetes (the NEFRON study). Med J Aust 2006;185:140-4.
- 15. Ito H, Oshikiri K, Mifune M, Abe M, Antoku S, Takeuchi Y, et al. The usefulness of the revised classification for chronic kidney disease by the KDIGO for determining the frequency of diabetic micro- and macroangiopathies in Japanese patients with type 2 diabetes mellitus. J Diabetes Complications 2012;26:286-90.
- Lee WR, Lim HS, Thai AC, Chew WL, Emmanuel S, Goh LG, et al. A window on the current status of diabetes mellitus in Singapore – the Diabcare-Singapore 1998 study. Singapore Med J 2001;42:501-7.
- Lee WR, Emmanuel S, Lim HS, Thai AC, Chew WL, Goh LG, et al. The status of diabetes mellitus in primary care institution and restructured hospitals in Singapore. Singapore Med J 2001;42:508-12.
- Wu AY, Kong NC, de Leon FA, Pan CY, Tai TY, Yeung VT, et al. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. Diabetologia 2005;48:17-26.
- American Diabetes Association. Standards of medical care in diabetes 2014. Diabetes Care 2014;37 Suppl 1:S14-80.
- Leng GC, Fowkes FG, Lee AJ, Dunbar J, Housley E, Ruckley CV. Use of ankle brachial pressure index to predict cardiovascular events and death: a cohort study. BMJ 1996;313:1440-4.

- 21. Tavintharan S, Ning Cheung, Su Chi Lim, Tay W, Shankar A, Shyong Tai E, et al. Prevalence and risk factors for peripheral artery disease in an Asian population with diabetes mellitus. Diab Vasc Dis Res 2009;6:80-6.
- 22. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimare glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130:461-70.
- Karter AJ, Ferrara A, Liu JY, Moffet HH, Ackerson LM, Selby JV. Ethnic disparities in diabetic complications in an insured population. JAMA 2002;287:2519-27.
- 24. Stanton RC. Clinical challenges in diagnosis and management of diabetic kidney disease. Am J Kidney Dis 2014;63:S3-21.
- 25. Disthabanchong S. Lowering vascular calcification burden in chronic kidney disease: is it possible? World J Nephrol 2013;2:49-55.
- 26. McCullough PA, Jurkovitz CT, Pergola PE, McGill JB, Brown WW, Collins AJ, et al. Independent components of chronic kidney disease as a cardiovascular risk state: results from the Kidney Early Evaluation

Program (KEEP). Arch Intern Med 2007;167:1122-9.

- The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-6.
- Bakris GL, Weir MR, Shanifar S, Zhang Z, Douglas J, van Dijk DJ. Effects of blood pressure level on progression of diabetic nephropathy: results from the RENAAL study. Arch Intern Med 2003;163:1555-65.
- Agency for Healthcare Research and Quality (AHRQ). 2012 National Healthcare Quality Report [Internet]. Rockville: AHRQ; 2013. Available at: http://www.ahrq.gov/research/findings/nhqrdr/nhqr12/index.html. Accessed 12 March 2014.
- Health and Social Care Information Centre (HSCIC). National Diabetes Audit – 2011-2012 [Internet]. Leeds: HSCIC; 2013. Available at: http:// www.hscic.gov.uk/searchcatalogue?productid=13129&q=%22National +diabetes+audit%22&sort=Relevance&size=10&page=1#top. Accessed 12 March 2014.